IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of	:	**Confirmation No. 5291**
Mie TAKAHASHI et al.	:	Attorney Docket No. 2001_1464A
Serial No. 09/937,730	:	Group Art Unit 1641
Filed January 8, 2002	:	Examiner Gary W. Counts
CHROMATOGRAPHY MEDIUM AND ITS MANUFACTURING METHOD	:	**Mail Stop: Appeal Brief-Patents**

REPLY BRIEF

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

THE COMMISSIONER IS AUTHORIZED TO CHARGE ANY DEFICIENCY IN THE FEE FOR THIS PAPER TO DEPOSIT ACCOUNT NO. 23-0975.

Sir:

This is a Reply Brief in response to the Examiner's Answer dated February 8, 2007.

As discussed in the Appeal Brief, Appellants' invention results in reduced influences to the reactive component (specific protein), reduced denaturation or deactivation of the reactive component, enhanced preservation stability of the chromatography medium, longer preservation period and relaxed maintenance conditions. It is known in the art to carry out surface active agent processing to avoid deterioration of permeability of the reaction layer and deterioration of solvability of the marker reagent. However, the surfactant used in the surface active agent processing causes the problems of deactivating the marker reagent or the reactive component (protein) which is immobilized in the reactive layer.

As also discussed in the Appeal Brief, the stereo-type structure of a protein is not likely to be destroyed in its dry state, in contrast to a protein in its solution state. If a surface active agent which holds water is used, then the reactive layer and the reactive component (protein) immobilized thereon will also include water, resulting in likely

denaturation of the reactive component (protein). Appellants have discovered that employing a surface active agent which is solidified when dried results in minimizing the denaturation and deactivation of the reactive component, thus enhancing preservation stability, extending quality maintenance and relaxing storage conditions.

However, it is difficult to maintain the preservation performance of a chromatography medium for a long period of time, even in a dry state. In the food industry, sugar is often used as a preservation stabilization agent. However, even if sugar is used, and even if the denaturation or deactivation of the reactive component (specific protein) is prevented, the solubility of sugar would result in deterioration of the permeability of the reaction layer.

Therefore, Appellants have discovered using a particular type of surface active agent, i.e., one which is solidified when dried and has a sugar in its hydrophilic part. Use of this particular type of surfactant results in preserving the permeability of the reaction layer for a long period of time, as well as protecting the specific proteins by the function of sugar, and preserving the performance of the specific proteins.

Appellants are not attempting to provide a surfactant molecule as a novel chemical material. Rather, Appellants have discovered a chromatography medium which employs a particular type of surfactant from among several thousand known surfactants. The surfactant of Appellants' invention can be found in a field that has no relation to that of the present invention, and thus would not be obvious to substitute in a composition such as Appellants' chromatography medium. Further, in a technical field of the present invention, as is represented by Chu (an immuno-chromatography apparatus), deactivation of an immobilized antibody occurs, and performance of a medium is deteriorated, resulting in shortened preservation period and stability of the medium. Appellants' objective with the present invention was to solve these problems.

Appellants assert that the combinations of references cited by the Examiner fail to teach or suggest Appellants' recited composition and method.

The Examiner states on page 7 of the Examiner's Answer that Appellants' arguments regarding Chu are not persuasive because it appears that Appellant is only arguing the reference of Chu, and not the combinations of references cited by the Examiner. Appellants respectfully disagree with the Examiner's position. This portion

of Appellants' arguments is intended to point out the distinctions between Chu and Appellants' invention. Further, this portion of Appellants' arguments discusses that Chu fails to provide motivation for the substitution of a surfactant which is solidified when dried and has a sugar in its hydrophilic part, from the broad field of known surfactants. As discussed in detail in the Appeal Brief, Appellants have discovered that using a surfactant which is solidified when dried and has a sugar in its hydrophilic part results in enhancing the permeability of the reaction layer, preserves the permeability of the reactive layer for a long time, and protects the reactive component from deactivation or denaturation. As Chu does not address the problem of achieving these advantages, Chu fails to provide motivation for the substitution set forth by the Examiner. Appellants also point to the detailed discussions on pages 9-17 of the Appeal Brief, where arguments relating to Chu in view of Nanbu et al. and Uenoyama et al. are clearly set forth.

The Examiner also states that the argument that Chu does not teach or suggest processing the entire reaction layer with a surface active agent is unpersuasive because Chu does teach that the entire reactive membrane is treated with a surfactant. The following comments are intended to clarify Appellants' point. Chu teaches that the receptor area, which is a limited region of the surfactant-treated porous reaction membrane, includes a higher concentration of surfactant than the peripheral areas. Since the limited receptor area has a higher concentration of surfactant, the liquid sample passes through this area faster than the peripheral areas. Thus, Chu strives for enhancement of assay sensitivity at a particular limited region of the reaction membrane. This disclosure differs from the goal of Appellants' invention, which is to enhance the permeability of the reaction layer (as a whole) by processing the entire reaction layer with a surface active agent.

Additionally, the Examiner states throughout the Examiner's Answer that the fact that Appellants have recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. Appellants respectfully disagree with the Examiner's assertion. The advantages to which the Examiner refers occur only when the Examiner picks Appellants' recited surfactant from among the large field of known surfactants. As discussed below, the only motivation for the Examiner to choose

Appellants' particular surfactant from the lists of surfactants disclosed by the references, is to look to Appellants' own disclosure for motivation. Further, as discussed in the Appeal Brief and below, the secondary references (Nanbu et al. and Uenoyama et al.) disclose many surfactants which would not achieve the advantages referred to by the Examiner. Thus, it can not be said that the advantages realized by Appellants' invention flow naturally from the teachings of the prior art.

Appellants assert that one of ordinary skill in the art would not have chosen a surfactant which is solidified when dried and which has a sugar in its hydrophilic part from the broad teachings of the cited references, without the benefit of Appellants' disclosure.

There are many types and kinds of known surfactants. Surfactants are known to have various characteristics and uses, such as detergent, foaming agent, emulsification agent, penetration agent, diffluence agent, dispersion agent, flexibility agent, retardant, spreading agent, sterilization agent, and agent for prevention of charging with electricity, to name a few.

The primary reference cited by the Examiner (Chu) belongs to a technical field that is similar to the present invention, and has a similar construction to Appellants' invention. Although Chu discloses surfactants (more than 30 different kinds), as admitted by the Examiner, the reference fails to teach or suggest a surfactant which satisfies Appellants' claims. Further, Chu fails to teach the effects achieved by using Appellants' particular surfactant.

As discussed in the Appeal Brief, the purpose of Appellants' invention is to provide a chromatography medium which can maintain the performance of the chromatography medium at high sensitivity and high precision, even when the chromatography medium is stored for a long period of time. Specifically, by employing a surfactant which is solidified when dried and has a sugar in its hydrophilic part, the permeability of the reactive layer is preserved for a long period of time, and the reactive component (specific proteins) is protected.

The Examiner has turned to two secondary references in an attempt to "find" a surfactant which may meet Appellants' requirements.

The Nanbu et al. reference relates to a method for measuring trypsin-inhibitor (UTI) included in urine. Nanbu et al. disclose that activity of a proteolytic enzyme is improved by containing a surfactant. On the other hand, Appellants' invention has no relation to the proteolytic enzyme. Further, Nanbu et al. disclose that the surfactant has no limitation in kind, and may be an ionic surfactant, an amphoteric surfactant, or a nonionic surfactant. Nanbu et al. do not place any criticality on the specific surfactant employed. Thus, many known surfactants are broadly disclosed by the Nanbu et al. reference. However, the Examiner fails to discuss, or even mention, most of the surfactants disclosed by the reference. Instead, the Examiner has picked and chosen from among the broad teachings of Nanbu et al., and has chosen to look only to a surfactant including sugar, in an attempt to satisfy Appellants' claims. However, the Examiner has provided no reason why one of ordinary skill in the art, reading the disclosure of Nanbu et al., would make this very specific choice.

Uenoyama et al. disclose a reaction system for measuring the concentration of urinary trypsin inhibitors comprising mixing a urine sample, a protease solution containing trypsin, and a buffer solution, adding a substrate and measuring the activity of an enzyme. Further, Uenoyama et al. provide a reaction system in which the dissolubility of a poorly-water soluble substrate is improved by using a surfactant. This invention is unrelated to Appellants' invention.

Uenoyama et al. disclose 16 kinds of surfactants as an amphoteric surfactant or a nonionic surfactant. However, only two surfactants of those taught by Uenoyama et al. are applicable to Appellants' invention. Thus, the remaining fourteen surfactants are inapplicable to Appellants' invention. However, the Examiner does not mention any of the non-applicable surfactants disclosed by the reference. Instead, similar to the discussion regarding Nanbu et al., the Examiner has picked and chosen from among the broad teachings of Uenoyama et al., and has chosen to look only to a surfactant including sugar, in an attempt to satisfy Appellants' claims. However, the Examiner has provided no reason why one of ordinary skill in the art, reading the disclosure of Uenoyama et al., would make this very specific choice.

The Examiner states, on page 8 of the Examiner's Answer, that the secondary references have been relied upon for teaching that the use of surfactants with sugar in a

hydrophilic part is known. However, merely establishing that these surfactants are known in the art does not establish a *prima facie* case of obviousness. At best, the Examiner has merely established that it would have been "obvious to try" various surfactants in the composition of Chu. The Court of Appeals for the Federal Circuit (hereafter "Federal Circuit") has repeatedly held that a case of *prima facie* obviousness is not established by demonstrating that a combination is "obvious to try". In In re Fine, the Board affirmed the Examiner's conclusion that it would have been obvious to substitute a nitric oxide detector for a sulfur dioxide detector in a system. However, the court held that the references disclosed, at most, that one skilled in the art might find it obvious to try the claimed invention, and that this is not a legitimate test of patentability. See In re Fine, 5 USPQ2d 1596 (Fed. Cir. 1988). A discussion that one skilled in the art might find it obvious to try various combinations is not the standard set forth in 35 U.S.C. § 103. See In re Geiger, 2 USPQ2d 1276 (Fed. Cir. 1987).

The Examiner is taking the position that it would be "obvious to try" any surfactant taught by Nanbu et al. or Uenoyama et al. in the composition of Chu. However, as discussed above, the Federal Circuit has repeatedly indicated that whether a particular combination is "obvious to try" is not a legitimate test of patentability.

Further, Appellants respectfully submit that one of ordinary skill in the art would not have chosen a surfactant which is solidified when dried and which has a sugar in its hydrophilic part from the broad teachings of the cited references, without the benefit of Appellants' disclosure. Thus, Appellants assert that the Examiner's rejection is based on hindsight, which is improper according to U.S. practice. "To imbue one of ordinary skill in the art with knowledge of the invention in suit, when no prior art reference or references of record convey or suggest that knowledge, is to fall victim to the insidious effect of a hindsight syndrome wherein that which only the inventor taught is used against its teacher... One cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention." See In re Fine.

Furthermore, in a recent decision, the Federal Circuit addressed the issue of hindsight. Specifically, the Federal Circuit stated:

> Most inventions arise from a combination of old elements and each element may often be found in the prior art.... However, mere identification in the prior art of each element is insufficient to defeat the patentability of the combined subject matter as a whole... Rather, to establish a *prima facie* case of obviousness based on a combination of elements discussed in the prior art, the Board must articulate the basis on which it concludes that it would have been obvious to make the claimed invention...
>
> When the Board does not explain the motivation, or the suggestion or teaching, that would have led the skilled artisan at the time of the invention to the claimed combination as a whole, we infer that the Board used hindsight to conclude that the invention was obvious.

See In re Kahn, 78 USPQ2d 1329 (Fed. Cir. 2006).

The Examiner broadly asserts that one of ordinary skill in the art would combine the teachings of the references because Nanbu et al. and Uenoyama et al. teach that surfactants improve assay sensitivity. However, it is not merely a matter of adding a surfactant to the teachings of Chu, as the Examiner's proposed combination implies. Rather, it is necessary for the Examiner to provide motivation as to (1) why one of ordinary skill in the art would replace a surfactant as disclosed by Chu with one taught by Nanbu et al. or Uenoyama et al., and (2) why one of ordinary skill in the art would specifically choose a surfactant which is solidified when dried and has a sugar in its hydrophilic part from the teachings of Nanbu et al. or Uenoyama et al. The Examiner has failed to provide the necessary motivation. In fact, based on the Examiner's statements, it is just as likely that one of ordinary skill in the art would choose a surfactant from the teachings of Nanbu et al. or Uenoyama et al. which is not solidified when dried and does not have a sugar in its hydrophilic part.

Therefore, based on the teachings of the cited references, the only reason one of ordinary skill in the art would substitute a surfactant which is solidified when dried and has a sugar in its hydrophilic part for a surfactant of Chu, is based on the teachings of Appellants' own disclosure. This is a case of impermissible hindsight.

There is no motivation, absent the use of Appellants' own disclosure, to choose a surfactant which is solidified when dried and has sugar in its hydrophilic part, for use in the teachings in Chu. At best, the Examiner has presented a situation where it might be obvious to try one of the surfactants of the secondary references in the disclosure of Chu, but this is not an appropriate standard for determining patentability. None of the cited references, nor a combination thereof, teach or suggest the objectives of Appellants' invention, nor provide any motivation to make the Examiner's suggested substitution.

Thus, for the reasons set forth in the Appeal Brief of November 17, 2006, and the reasons set forth above, it is asserted that the subject matter of Appellants' claims is clearly patentable over the cited combinations of references. The Board of Patent Appeals and Interferences is respectfully requested to find in favor of Appellants.

Respectfully submitted,

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